

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 16 NOV 2005

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| Applicant's or agent's file reference NC-290 | FOR FURTHER ACTION | | See Form PCT/IPEA/416 | | | | | | | | | | | | | | | | | | | | | | | | |
| International application No. PCT/JP2004/019451 | International filing date (day/month/year) 17.12.2004 | Priority date (day/month/year) 26.12.2003 | | | | | | | | | | | | | | | | | | | | | | | | | |
| International Patent Classification (IPC) or national classification and IPC C07D215/14, A61K31/47 | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Applicant NISSAN CHEMICAL INDUSTRIES, LTD. et al. | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 5 sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: <ol style="list-style-type: none"> a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows: <ul style="list-style-type: none"> <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <ol style="list-style-type: none"> 4. This report contains indications relating to the following items: <table style="width: 100%; border: none;"> <tr> <td style="width: 10%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td>Basis of the opinion</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | | | | <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | <input type="checkbox"/> | Box No. II | Priority | <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | | | |
| Date of submission of the demand 23.06.2005 | | Date of completion of this report 14.11.2005 | | | | | | | | | | | | | | | | | | | | | | | | | |
| Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div> | | Authorized Officer Bakboord, J Telephone No. +49 89 2399- 2768 | | | | | | | | | | | | | | | | | | | | | | | | | |



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/JP2004/019451

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-14 as originally filed

Claims, Numbers

1-4 as originally filed

Drawings, Sheets

1/1 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/JP2004/019451

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-----|
| Novelty (N) | Yes: Claims | 1-4 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-4 |
| Industrial applicability (IA) | Yes: Claims | 1-4 |
| | No: Claims | |

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The present invention relates to a crystal form of pitavastatin calcium.

V.2 Reference is made to the following documents:

D1: WO 03/016317 A

D2: EP-A-0 520 406, cited in the application

D3: SUZUKI M ET AL: "First Systematic Chiral Syntheses of Two Pairs of Enantiomers with 3,5-dihydroxyheptenoic Acid Chain, Associated with a Potent Synthetic Statin NK-104" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 9, no. 20, 18 October 1999 (1999-10-18), pages 2977-2982, XP004180521 ISSN: 0960-894X, cited in the application

D4: DRUGS OF THE FUTURE, vol. 23, no. 8, 1998, pages 847-859, XP009047388

D5: WO 2004/072040 A (CIBA SPECIALTY CHEMICALS HOLDING INC; VAN DER SCHAAF, PAUL, ADRIAAN; B) 26 August 2004 (2004-08-26)

Document D5 was published after the priority date. In the assumption that the priority is valid this document is not regarded as prior art.

V.3 Novelty

Document D1 discloses a crystal form of pitavastatin calcium. No water seems to be present in the crystal (examples 9 and 10).

Document D2 discloses a calcium salt of pitavastatin. No water is mentioned (example 3).

Document D3 discloses a calcium salt of pitavastatin. No water seems to be present (compounds 1b and 1d).

Document D4 discloses a calcium salt of pitavastatin. No water is mentioned (compound 8).

It is noted that document D5 discloses a form A crystal of pitavastatin calcium. It is mentioned that form A can contain up to 15% water. Form A is prepared from pitavastatin sodium upon reaction with CaCl_2 in an aqueous reaction medium.

Crystal form A of pitavastatin calcium containing 5 to 15% water is disclosed in none of the documents. Claim 1 therefore fulfills the requirements of Art 33(2) PCT.

Claim 2 describes a process for the preparation of the crystal of claim 1 and is novel by consequence.

Claim 3 describes a process for producing a drug substance of the crystal of claim 1 and is novel by consequence.

Claim 4 describes a pharmaceutical composition containing the crystal of claim 1 and is novel by consequence.

V.4 Inventive step

Starting from documents D1-D4 the problem to be solved by the present application may be regarded as how to provide a novel crystal form of pitavastatin having improved properties. As no data are present in the application to show the surprising effect of the crystals of the invention no inventive step can at present be acknowledged (Art 33(3) PCT).

VI Certain documents cited

WO 2004/072040 A